



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/670,958	09/25/2003	Alan M. Kleinfeld	FFASC.063A	7040
20995	7590	02/09/2005	EXAMINER	
KNOBBE MARTENS OLSON & BEAR LLP			SMITH, ZANDRA V	
2040 MAIN STREET			ART UNIT	
FOURTEENTH FLOOR			PAPER NUMBER	
IRVINE, CA 92614			2877	

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/670,958	Applicant(s) KLEINFELD ET AL.	
	Examiner Zandra V. Smith	Art Unit 2877	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 September 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-82 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 80-82 is/are allowed.
- 6) ☐ Claim(s) 1-20, 23-69, 71 and 75 is/are rejected.
- 7) ☒ Claim(s) 21, 22, 70, 72-74 and 76-79 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>01/22/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Information Disclosure Statement

The Information Disclosure Statement filed 22 December 2003 has been entered in the application and the references considered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 8-9, 14-15, 17-18, 23, 25-26, 28-29, 31-32, 35-36, 39, 47-48, 50, 54, 58, 65-68, and 71 are rejected under 35 U.S.C. 102(b) as being anticipated by *Robertson, Jr. et al.* (4,833,332).

As to **claims 1, 47, and 71**, Robertson, Jr. discloses a scanning fluorescent detection system, comprising:

a sample receptacle (col. 7, lines 5-10); an excitation source (30); a first detector to detect first emission in a first bandwidth (52); a second detector to detect second emission in a second bandwidth (54); and a processor (80) to calculate a ratio (col. 4, lines 25-40) of the emissions.

As to **claims 2-3**, Robertson, Jr. discloses everything claimed, as applied above, in addition a first optical filter (58, col. 11, lines 1-20) is provided.

As to **claims 8-9**, Robertson, Jr. discloses everything claimed, as applied above, in addition a second optical filter is provided (col. 11, lines 1-20).

As to **claims 14-15**, Robertson, Jr. discloses everything claimed, as applied above, in addition an optical excitation filter is provided (34).

As to **claims 17-18**, Robertson, Jr. discloses everything claimed, as applied above, in addition a Xenon Arc lamps, which is a broadband light source, is provided (col. 9, line 58).

As to **claim 23**, Robertson, Jr. discloses everything claimed, as applied above, in addition a first analog to digital converter (70) and a second analog-to-digital converter (72) are provided, wherein the processor calculates the ratio of the signal based on outputs from the analog-to-digital converters (col. 12, line 65-col. 13, line 2).

As to **claims 25-26, 28**, Robertson, Jr. discloses everything claimed, as applied above, in addition an output device is provided, computer (col. 13, line 64 and col. 14, lines 1-5), which inherently includes a display device.

As to **claim 29**, Robertson, Jr. discloses everything claimed, as applied above, in addition the concentration of a molecule in a sample is determined based on the ratio (col. 13, lines 10-25).

As to **claims 31-32**, Robertson, Jr. discloses everything claimed, as applied above, in addition an optical detector is provided (photomultiplier tube, col. 11, line 2).

As to **claims 35-36**, Robertson, Jr. discloses everything claimed, as applied above, in addition the first detector is positioned on an axis different from an axis of the excitation emission and the axis of the first sample emission is the same as an axis of excitation emission (see fig. 2).

As to **claims 39, 58, and 65-68**, Robertson, Jr. discloses a scanning fluorescent detection system, comprising:

Art Unit: 2877

a sample receptacle (30), a first filter (58), a first detector (52), a first analog-to-digital converter (70), a second filter (58), a second detector (54), a second analog-to-digital converter (72), and a processor (80) configured to calculate a ratio based on the outputs of the detectors (col. 9, line 55-col. 10, line 35, col. 11, line 1-15, col. 12, lines 60-65 and col. 13, lines 10-28).

As to **claim 48**, Robertson, Jr. discloses everything claimed, as applied above, in addition the light source has an emission in a 350-400 nm range (col. 9, lines 57-62).

As to **claims 50 and 54**, Robertson, Jr. discloses everything claimed, as applied above, in addition detecting the emission from the sample includes filtering and emission, detecting an output and converting to a digital representation (col. 12, line 58- col. 13, line 10).

As to **claim 72**, Robertson, Jr. discloses everything claimed, as applied above, in addition the first bandwidth comprises a first interference absorbance bandwidth and a second interference bandwidth (col. 11, lines 40-50)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 4-7, 10-13, 16, 19-20, 24, 27, 33-34, 40-41, 49, 51-53, 55-57, 59-61, 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Robertson, Jr. et al. (4,833,332)*.

As to **claims 4-7, 10-13, 16, 40-41, 51-53, 55-57, 59-61** Robertson, Jr. discloses everything claimed, as applied above, with the exception of the wavelengths of the filter, however Robertson, Jr. does state that the filters have passbands of the dyes used (col. 11, lines

Art Unit: 2877

30-35 and 49-52) and that other filters may be used to accommodate other dyes (col. 11, lines 49-50). It would have been obvious to one having ordinary skill in the art at the time of invention to provide filters with passbands and bandwidths claimed to accommodate the dyes used and to ensure the detection of the component of interest.

As to **claims 19 and 49**, Robertson, Jr. discloses everything claimed, as applied above, with the exception of a narrowband light source, however to do so would have been obvious to one having ordinary skill in the art at the time of invention since the light is selected to provide an excitation beam of radiation (3) with a wavelength determined by the fluorophores of interest (col. 9, lines 58-60), the use of a narrowband light source would excite only the fluorophores of interest.

As to **claim 20**, Robertson, Jr. discloses everything claimed, as applied above, with the exception of a LED as the light source, however it would have been obvious to one having ordinary skill in the art at the time of invention to use an LED since LED's are inexpensive and easily controllable to provide the desired wavelengths.

As to **claim 24**, Robertson, Jr. discloses everything claimed, as applied above, with the exception of a memory, however since a computer (col. 13, line 64) is provided which typically includes a memory and since results are compared, it would have been obvious to one having ordinary skill in the art at the time of invention to provide a means to store measured data for later use.

As to **claim 27**, Robertson, Jr. discloses everything claimed, as applied above, with the exception of the output device being a display or a printer, however since a computer (col. 13, line 64) is used and since a computer the inclusion of a printer is well known and the use of a

Art Unit: 2877

printer would provide a hard copy of the result, it would have been obvious to one having ordinary skill in the art at the time of invention to include a printer.

As to **claims 33-34**, Robertson, Jr. discloses everything claimed, as applied above, with the exception of a photodiode or CCD, however since both are examples of optical detection device it would have been obvious to one having ordinary skill in the art at the time of invention to use a photodiode or CCD as a means to detect and convert the optical signal into an electrical signal.

As to **claim 69**, Robertson, Jr. discloses everything claimed, as applied above, in addition a ration is determined (col. 12, line 65- col. 132, line 10). Robertson, Jr. differs from the claimed invention in that the coefficient of variation is not disclosed, however it would have been obvious to one having ordinary skill in the art at the time of invention to have a small coefficient of variation in the measurement to ensure that the measurement does not significantly deviate from the desired result.

Claims 1, 30, 37-38, 44-46, 58, 62-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Robertson, Jr. et al. (4,833,332)* in view of *Kleinfeld (5,470,714)*.

As to **claims 1, 30, 37-38, 44**, Robertson, Jr. discloses a scanning fluorescent detection system, comprising:

a sample receptacle (col. 7, lines 5-10); an excitation source (30); a first detector to detect first emission in a first bandwidth (52); a second detector to detect second emission in a second bandwidth (54); and a processor (80) to calculate a ratio (col. 4, lines 25-40) of the emissions. Robertson, Jr. differs from the claimed invention in that the first fluorescent signal does not come from a molecule bound to a ligand of free fatty acid in a sample and the second fluorescent

Art Unit: 2877

signal does not come a molecule unbound to a ligand of free fatty acid in a sample. However Kleinfeld discloses a method of determining the free fatty acid in a sample that includes measuring fluorescence from a molecule bound to a ligand of free fatty acid in a sample and a molecule unbound to a ligand of free fatty acid in a sample (col. 4, lines 15-30) that includes determination of a ratio of the fluorescent signals (col. 8, lines 1-25). Kleinfeld does not disclose the particular apparatus for the measurement but does disclose that the apparatus is not a critical limiting factor of the invention (col. 6, lines 30-35). Therefore, it would have been obvious to one having ordinary skill in the art at the time of invention to use the apparatus as disclosed by Robertson, Jr. to perform the method as disclosed by Kleinfeld since Robertson, Jr. provides a system for measuring two fluorescent signals from a sample and determining a ratio of the results to determine a component of a sample and since the determination of free fatty acid is important in the diagnosis of treatment of disease or in studying causes or effects of disease.

As to **claims 45-46 and 63**, the system of Robertson, Jr. and Kleinfeld disclose everything claimed, as applied above, in addition Kleinfeld discloses the use of ADIFAB and ADIFAB2 (col. 5, lines 20-50). It would have been obvious to one having ordinary skill in the art at the time of invention to use ADIFAB and ADIFAB2 since they exhibit different fluorescence when bound that when unbound to FFA in a sample.

As to **claims 58, 62 and 64**, Robertson, Jr. discloses a scanning fluorescent detection system, comprising:

a sample receptacle (30), a first filter (58), a first detector (52), a first analog-to-digital converter (70), a second filter (58), a second detector (54), a second analog-to-digital converter

Art Unit: 2877

(72), and a processor (80) configured to calculate a ratio based on the outputs of the detectors (col. 9, line 55-col. 10, line 35, col. 11, line 1-15, col. 12, lines 60-65 and col. 13, lines 10-28).

Robertson, Jr. differs from the claimed invention in that the first fluorescent signal does not come from a molecule bound to a ligand of free fatty acid in a sample and the second fluorescent signal does not come a molecule unbound to a ligand of free fatty acid in a sample. However Kleinfeld discloses a method of determining the free fatty acid in a sample that includes measuring fluorescence from a molecule bound to a ligand of free fatty acid in a sample and a molecule unbound to a ligand of free fatty acid in a sample (col. 4, lines 15-30) that includes determination of a ratio of the fluorescent signals (col. 8, lines 1-25). Kleinfeld does not disclose the particular apparatus for the measurement but does disclose that the apparatus is not a critical limiting factor of the invention (col. 6, lines 30-35). Therefore, it would have been obvious to one having ordinary skill in the art at the time of invention to use the apparatus as disclosed by Robertson, Jr. to perform the method as disclosed by Kleinfeld since Robertson, Jr. provides a system for measuring two fluorescent signals from a sample and determining a ratio of the results to determine a component of a sample and since the determination of free fatty acid is important in the diagnosis of treatment of disease or in studying causes or effects of disease.

Claim 71 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Robertson, Jr. et al.* (4,833,332) in view of *Wolfbeis et al.* (4,580,059).

As to **claim 71**, Robertson, Jr. discloses everything claimed, as applied above, with the exception of verifying the accuracy of the target molecule, however to do so is well known as taught by Wolfbeis. Wolfbeis discloses a method for fluorometric determination that includes calibration to verify the accuracy of measurement (col. 1, lines 55-62). It would have been

Art Unit: 2877

obvious to one having ordinary skill in the art at the time of invention to calibrate the system and verify the accuracy of the measurement to ensure that the system is properly identifying the molecules.

Allowable Subject Matter

Claims 80-82 are allowable over the prior art of record.

Claims 21-22, 70, 72-74 and 76-79 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: the prior art of record, taken alone or in combination fails to disclose or render obvious imaging optics (claim 21), a temperature sensor (70), determining in a calibrating ratio fluorometer a ratio of fluorescence of a sample, determining in a second ratio fluorometer an uncorrected ratio of fluorescence of the sample, and adjusting a detector output such that the uncorrected ratio of fluorescence is equal to the ratio of fluorescence (claim 80), in combination with the rest of the limitations of claim.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Rao et al. (US 6,563,585 B1) disclose a ratiometric fluorometer.

Art Unit: 2877

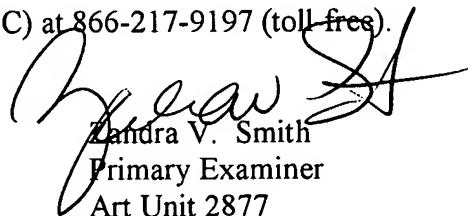
Fax/Telephone Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zandra V. Smith whose telephone number is (571) 272-2429.

The examiner can normally be reached on 8:00 a.m. - 4:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gregory J. Toatley Jr. can be reached on (571) 272-2800 ext. 77. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).


Zandra V. Smith
Primary Examiner
Art Unit 2877

Saturday, February 05, 2005